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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/716,704
Filing Date: November 20, 2003
Appellant(s): SOITO ET AL.

Theodore R. Allen
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 04/05/2007 appealing from the Office action mailed 10/13/2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

6,413,228	Hung et al	07-2002

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

1. **Claims 17-23 & 26** are rejected under 35 U.S.C. 102(e) as being anticipated by Hung et al. (US Patent No. 6,413,228).

2. In regards to **Claim 17**, Hung et al disclose a system of cytological evaluation of epithelial cells collected from a human breast duct (Col.28: 60-67; Col.29: 1-9) comprising:

a tool or apparatus 30 best seen in Figure 3, for accessing a breast duct and collecting breast duct fluid from a human breast while the tool is in the duct (Col.1: 1-17; Col.18: 24-28);

a chart or written guidelines, i.e. in the form of published methods (Col.13: 66-67; Col.14: 1-42) for evaluating the ductal epithelial cells in the sample (Col.24: 37-45; Col.25: 17-33) for one or more observed indicia selected from the group consisting of cell grouping (Col.13: 54-55), cell shape, cell size (Col.25: 10-13), nuclear size, nuclear shape, presence or absence of nucleoli, nuclear-to-cytoplasmic ratio, vacuoles in the cytoplasm, cytoplasmic shape, cytoplasmic border, presence or absence of anisonucleosis, presence or absence of mitotic figures, nuclear membrane quality, presence of necrotic debris, chromatin distribution, coarseness of chromatin (Col.13: 51-58), and the presence or absence of microcalcifications;

an algorithm for classifying the sample as being normal, atypical or malignant based on the observed indicia (Col.24: 45-51; Col.26: 35-48), for example, classifying the sample as atypical sample when cellular abnormalities, increased coarseness of the chromatin, and tendency for more single cells as well as groups of cells are present (Col.13: 51-63).

3. In regards to **Claim 18**, Hung et al disclose the tool or apparatus for accessing a breast duct comprises a breast duct access and fluid and cell retrieval tool, and one or more of a probe,

a tool for administering anesthetic, marking tools for marking an accessed or fluid yielding duct, or a collection receptacle for collecting retrieved fluid and cells (Col.18: 24-Col.19: 15).

4. In regards to **Claim 19**, Hung et al disclose the algorithm classifies the sample as malignant when the sample is characterized by at least an identifying feature selected from the group consisting of a loss of cell cohesiveness, loose clusters of epithelial cells, enlarged cells, enlarged nuclei, high nuclear-to-cytoplasmic ratio, increased cytoplasm in some cells, irregular nuclear membranes, clumped chromatin, hyperchromatic chromatin, unevenly dispersed chromatin, enlarged nucleoli, multiple nucleoli, marked variation among the cells of the sample in cell size and nuclear size, necrotic debris, and microcalcifications in background material appearing as dense material with smooth borders and concentric layers or dystrophic and amorphous (Col.13: 51-67; Col.14: 1-42; Col.25: 1-33).

5. In regards to **Claim 20**, Hung et al disclose the algorithm classifies the sample as atypical with marked changes when the sample is characterized by at least an identifying feature selected from the group consisting of enlarged ductal epithelial cells, marked nuclear increase in ductal epithelial cells, variation in size and shape of the ductal epithelial cells as compared to normal ductal epithelial cells, abundant cytoplasm in some cells, decreased nuclear-to-cytoplasmic ratios in some cells, coarse chromatin, mild abnormality in chromatin distribution, larger nucleoli than in normal cells, multiple nucleoli, more prominent nucleoli, groups of nuclei that appear to be overlapping, and mitotic figures (Col.13: 51-67; Col.14: 1-42; Col.25: 1-33).

6. In regards to **Claim 21**, Hung et al disclose the algorithm classifies the sample as atypical with mild changes when the sample is characterized by at least some of an identifying feature selected from the group consisting of single ductal cells, cohesive multilayered cells, complex

groups of cells, monolayered cells, an increased number of cell layers compared to normal cells, increased overlapping of the cells, nuclear crowding of cells, minimally enlarged cells, moderate increase in nuclear size to within a range from about 12 to about 16 .mu.m in diameter, slight anisonucleosis in some cells, and presence of nucleoli (Col.13: 51-67; Col.14: 1-42; Col.25: 1-33).

7. In regards to **Claim 22**, Hung et al disclose the algorithm classifies the sample as normal when the sample is characterized by at least some of an identifying feature selected from the group consisting of single cells, monolayer sheets, tight cells clusters usually one or two cell layers thick, small nuclei in a size range from about 8 to about 12 .mu.m in diameter, high nuclear-to-cytoplasmic ratio depending on the orientation of the cells in clusters, in single cells a columnar shape of cytoplasm, in single cells discreet small vacuoles in the cytoplasm, in single cells discreet cytoplasmic border, cohesive groups of ductal epithelial cells with cells of uniform size and regular round to oval shape, monolayer sheets of cells with uniform, small cells, and monolayer sheets of cells with small inconspicuous nucleoli (Col.13: 51-67; Col.14: 1-42; Col.25: 1-33).

8. In regards to **Claim 23**, Hung et al disclose the algorithm inherently classifies the sample as insufficient cells to make a diagnosis (ICMD) when the sample has fewer than 10 epithelial cells (Col.33: 28-30) due to the fact that cell clusters of less than 10 are not even evaluated and classified as best seen in Table 1.

9. In regards to **Claim 26**, Hung et al disclose a system of cytological evaluation of epithelial cells collected from a human breast duct (Col.28: 60-67; Col.29: 1-9) comprising:

a tool or apparatus 30 best seen in Figure 3, for accessing a breast duct and collecting breast duct fluid from within the breast duct (Col.1: 1-17; Col.18: 24-28), said tool comprising an elongated portion shaped and sized for extending into the breast duct comprising a single elongated internal lumen through which fluid can be introduced and received from within the breast duct, best seen in Figures 3, 4d, and 7;

a chart or written guidelines, i.e. in the form of published methods (Col.13: 66-67; Col.14: 1-42) for evaluating the ductal epithelial cells in the sample (Col.24: 37-45; Col.25: 17-33) for one or more observed indicia selected from the group consisting of cell grouping (Col.13: 54-55), cell shape, cell size (Col.25: 10-13), nuclear size, nuclear shape, presence or absence of nucleoli, nuclear-to-cytoplasmic ratio, vacuoles in the cytoplasm, cytoplasmic shape, cytoplasmic border, presence or absence of anisonucleosis, presence or absence of mitotic figures, nuclear membrane quality, presence of necrotic debris, chromatin distribution, coarseness of chromatin (Col.13: 51-58), and the presence or absence of microcalcifications;

an algorithm for classifying the sample as being normal, atypical or malignant based on the observed indicia (Col.24: 45-51; Col.26: 35-48), for example, classifying the sample as atypical sample when cellular abnormalities, increased coarseness of the chromatin, and tendency for more single cells as well as groups of cells are present (Col.13: 51-63).

(10) Response to Argument

10. Appellant's arguments filed 04/05/2007 have been fully considered but they are not persuasive. Appellant argues the anticipatory rejection of Claims 17-23 and 26 under Hung et al.

The Examiner disagrees and maintains the rejection, noting the following in response to Appellants arguments:

11. Appellant contends that the Final Rejection dated 10/13/2006 is improper for citing portions of the reference not specifically cited in the Non Final Office Action dated 05/12/2006. However, it is noted that the same reference is used for the rejection throughout prosecution and it is understood that its contents are taken in its entirety and thus do not constitute a new grounds of rejection.

12. Appellant contends that there is no mention of charts or written guidelines for evaluating the cell sample and that the "published methods" of Hung et al (Col.13: 66-67; Col.14: 1-42) fail to qualify as an equivalent of Appellant's written guidelines because guidelines are non-subjective and published methods are merely variable experimental protocol used to assist in research. However, it is noted that since Appellant has failed to at least specifically define the desired meaning of said charts or written guidelines in the specification (mentioned only in ¶0025, 0031, and 0047), the rather specific definition of guidelines above does not preclude a broad reasonable interpretation of said term to encompass both the allegedly subjective experimental nature of published methods as well as the more non-subjective kind as defined by "a statement or other indication of policy or procedure by which to determine a course of action" (www.dictionary.com). In fact, Hung et al explicitly state that said published methods give "guidance" to the analysis of the ductal epithelial cells (Col.14: 13-15), thus suggesting that said published methods are widely relied upon to the extent to surpass a mere variable experimental protocol and thus qualify as a "guideline."

13. Furthermore, it is also noted that said claims (Claims 17 and 26) merely recite " a chart or written guidelines for evaluating the ductal epithelial cells in the sample *for one or more observed indicia selected from the group consisting of...*" [emphasis added]. Such language merely requires that the chart or written guidelines be used to evaluate *the presence or absence* of said observed indicia, which Hung et al clearly disclose (at least in Col.13: 42-63) and thus invalidate any arguments pertaining to the purported subjective or non-subjective nature of said published methods as irrelevant. Thus, it is shown that Hung et al anticipate a chart or written guidelines for evaluating the ductal epithelial cells in the sample for one or more observed indicia as claimed.

14. Appellant contends that that is no mention of an algorithm for classifying a sample as being normal, atypical or malignant based upon observed indicia and that the word "algorithm" does not appear anywhere in the specification of Hung et al. As noted in the Final Rejection, the Examiner reiterates that the mere fact that the word "algorithm" does not appear in the specification of Hung et al does not mean that an algorithm, defined as Hung et al do not disclose "a set of rules for solving a problem in a finite number of steps". In response to this, Appellant contends that Hung et al do not teach or suggest any steps or set of rules to solve a problem. However, the Examiner points out that Hung et al clearly disclose a methodology used to diagnose or establish the condition of the cell sample as being normal, atypical, or malignant (Col.24: 45-51; Col.26: 35-48), wherein said methodology must necessarily contain at least one rule with at least one finite step to arrive at the diagnostic conclusion of the cell sample being classified as normal, atypical, or malignant, which therefore constitutes said methodology as an algorithm as broadly defined above and in ¶0047 of Appellant's specification (i.e. a flow or

decision chart having at least one rule and one step). It is noted that Appellant fails to expand upon the exact definition of said algorithm at least in the specification, aside from the mentioning found in ¶0047.

15. Furthermore, it is also noted that Hung et al clearly disclose at least one specific rule having at least one finite step to classify the cell sample, for example, a rule and step of diagnosing the cell sample as atypical sample when cellular abnormalities, increased coarseness of the chromatin, and tendency for more single cells as well as groups of cells are present (Col.13: 51-63). Thus, it is shown that Hung et al clearly anticipate an algorithm for classifying the sample as being normal, atypical or malignant as claimed.

16. Lastly, Appellant contends that Hung et al do not disclose all the elements combined to make the system of the present invention and that Hung et al purportedly only disclose each element in isolation. However, it is noted that Hung et al clearly teach a cytological evaluation kit comprising a medical tool to access the breast duct and instructions on how to analyze the collected cell sample, i.e. cytological identification of cellular characteristics and making other assessments of the sample, i.e. classifying (Col.28: 60-67; Col.29: 1-14) in the aforementioned manner and thus anticipate a system comprising a tool, a chart or written guidelines, and an algorithm as claimed and defined and elaborated above.

17. Regarding Claim 23, Appellant contends that the lack of mention of an algorithm for determination of cell sample sufficiency and that Column 33, lines 28-30 merely define cell clusters as having greater than 10 cells. However, it is noted that due to the fact that all the cell clusters sampled and analyzed by the algorithm as explained above must necessarily contain 10

cells as shown in Table 1, it is inherent that a sample cell cluster with less than 10 cells would not even be analyzed and thus constitute a classification of insufficient for diagnosis.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/HQN/
Helen Nguyen
Examiner, Art Unit 3736

Conferees:

Max Hindenburg

Angela Sykes